

What is claimed is:

1. An composition comprising a first insulin species and a second insulin species, wherein the first insulin species and the second insulin species form a heterodimeric complex; and wherein the first insulin species and the second insulin species are selected such that the heterodimeric complex is more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species.
2. The composition of claim 1, wherein the first insulin species is human insulin and the second insulin species is a variant of human insulin having at least one amino acid substitution.
3. The composition of claim 2, wherein the variant of human insulin is LISPRO insulin.
4. The composition of claim 3, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.
5. The composition of claim 4, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.
6. The composition of claim 1, wherein the composition is a pharmaceutical composition.
7. The composition of claim 1, wherein the heterodimeric complex formed by the first insulin species and the second insulin species is determined to be more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species by a spectrophotometric assay of turbidity.
8. The composition of claim 1, wherein the heterodimeric complex formed by the first insulin species and the second insulin species is shown to be more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species by a Thioflavin-T assay.

9. A composition comprising a combination of a first insulin species and a second insulin species, wherein the first and second insulin species are selected to generate a composition that is more stable than a composition having only the first insulin species or a composition having only the second insulin species.

10. The composition of claim 1, wherein the first insulin species is human insulin and the second insulin species is a variant of human insulin having at least one amino acid substitution.

11. The composition of claim 10, wherein the variant of human insulin is LISPRO insulin.

12. The composition of claim 11, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.

13. The composition of claim 12, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.

14. The composition of claim 9, wherein the composition is a pharmaceutical composition.

15. A method of making an insulin composition, comprising combining a first insulin species and a second insulin species, wherein the first insulin species and the second insulin species form a heterodimeric complex; and wherein the first insulin species and the second insulin species are selected such that the heterodimeric complex is more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species.

16. The method of claim 15, wherein the first insulin species is human insulin and the second insulin species is a variant of human insulin having at least one amino acid substitution.

17. The method of claim 16, wherein the variant of human insulin is LISPRO insulin.

18. The method of claim 17, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.

5 19. The method of claim 12, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.

10 20. The method of claim 15, wherein the composition is a pharmaceutical composition.

15 21. A method of stabilizing an insulin composition, comprising combining a first insulin species and a second insulin species, wherein the first and second insulin species are selected to generate a composition that is more stable than a composition having only the first insulin species or a composition having only the second insulin species.

20 22. The method of claim 21, wherein the first insulin species is human insulin and the second insulin species is a variant of human insulin having at least one amino acid substitution.

25 23. The method of claim 22, wherein the variant of human insulin is LISPRO insulin.

30 24. The method of claim 23, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.

25 25. The method of claim 24, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.

26. The method of claim 25, wherein the composition is a pharmaceutical composition.

30 27. A method for identifying a stabilized insulin composition comprising the steps of combining a first insulin species with a second insulin species so that a heterodimeric complex formed from the

first and second insulin species is generated, comparing the stability of the heterodimeric complex formed from the first and second insulin species with the stability of a homodimeric complex formed from the first insulin species or a homodimeric complex formed from the second insulin species and identifying a formulation wherein the heterodimeric complex formed from the first and second insulin species is more stable than homodimeric complex formed from the first insulin species or a homodimeric complex formed from the second insulin species.

28. The method of claim 27, wherein the heterodimeric complex formed by the first insulin species and the second insulin species is shown to be more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species in a spectrophotometric assay of turbidity.

29. The method of claim 27, wherein the heterodimeric complex formed by the first insulin species and the second insulin species is shown to be more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species in an assay with Thioflavin-T.

30. A method for identifying a stabilized insulin composition comprising the steps of combining a first insulin species with a second insulin species and comparing the stability of the formulation having a combination of the first and second insulin species with the stability of a formulation having only the first insulin species or a formulation having only the second insulin species and identifying an insulin composition wherein the formulation generated by combining the first and second insulin species is more stable than a formulation having only the first insulin species or a formulation having only the second insulin species.

31. The method of claim 30, wherein the formulation having a combination of the first and second insulin species is determined to be more stable than a formulation having only the first insulin species or a formulation having only the second insulin species by a spectrophotometric assay of turbidity.

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Year	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	